CLAIMS

We claim:

1. A compound comprising hyaluronan cross-linked with a polyfunctional cross-linking agent having two or more aziridines selected from the group consisting of 1,1',1''-methylidynetris-aziridine; 1,1',1''-methylidynetris[2,2-dimethyl]-aziridine; 1,1'-[2-(1-aziridinylmethyl)-1,3-propanediyl]bis-aziridine; 1-aziridinepropanoic acid, 2,2-bis[[3-(1-aziridinyl)-1-oxopropoxy]methyl]-1,3-propanediyl ester; 1-aziridinepropanoic acid, 2-propyl-, 2-(hydroxymethyl)-2-[[1-oxo-3-(2-propyl-1-aziridinyl)propoxy]methyl]-1,3-propanediyl ester; 1-aziridinepropanoic acid, 2,2-dimethyl-, 2-[[3-(2,2-dimethyl-1-aziridinyl)-1-oxopropoxy]ethyl]-2-(hydroxymethyl)-1,3-propanediyl ester; di[2-(1-aziridinyl)ethyl)]adipate; 1,3-bis(1-aziridinyl)-3-phenyl-1-propanol; 1,1'-(1,3-propanediyl)bis-2-aziridinecarbonitrile; α, β-bis(1-aziridinyl) 2-furanpropanol; 1-[3-(1-aziridinyl)propionyl]-aziridine; 1,3-bis(1-aziridinyl)-2-propanol; 1,3-bis(2-methyl-1-aziridinyl)-2-propanol; (1-aziridinylpyruvoyl)-,1-[(p-nitrophenyl)hydrazone] aziridine; and 1,1'-(1,3-dioxo-1,3-propanediyl) bis-aziridine, wherein the equivalent ratio of hyaluronan to aziridine is 1:1 to 1:10.

2. The compound of claim 1, wherein the equivalent ratio of hyaluronan to aziridine is 1:3 to 1:10.

3. The compound of claim 1, wherein the equivalent ratio of hyaluronan to aziridine is 1:3 to 1:5.

4. The compound of claim 1, wherein the equivalent ratio of hyaluronan to aziridine is 1:4 to 1:5.

5. The compound of claim 1 wherein the molecular weight of the hyaluronan is 500 kDaltons or more.

6. The compound of claim 1 wherein the polyfunctional cross-linking agent is di[2-(1-aziridinyl)ethyl)]adipate.

7. A process of making a compound comprising hyaluronan cross-linked with a polyfunctional cross-linking agent having two or more aziridines selected from the group consisting of 1,1',1''-methylidynetris-aziridine; 1,1',1''-methylidynetris[2,2-dimethyl]-aziridine; 1,1'-[2-(1-aziridinylmethyl)-1,3-propanediyl]bis-aziridine; 1-aziridinepropanoic acid, 2,2-bis[[3-(1-aziridinyl)-1-oxopropoxy]methyl]-1,3-propanediyl ester; 1-Aziridinepropanoic acid, 2-propyl-, 2-(hydroxymethyl)-2-[[1-oxo-3-(2-propyl-1-aziridinyl)propoxy]methyl]-1,3-propanediyl ester; 1-aziridinepropanoic acid, 2,2-dimethyl-, 2-[[3-(2,2-dimethyl-1-aziridinyl)-1-oxopropoxy]ethyl]-2-(hydroxymethyl)-1,3-propanediyl ester; di[2-(1-aziridinyl)ethyl)]adipate; 1,3-bis(1-aziridinyl)-3-phenyl-1-propanol; 1,1'-(1,3-propanediyl)bis-2-aziridinecarbonitrile; α, β-bis(1-aziridinyl) 2-furanpropanol; 1-[3-(1-aziridinyl)propionyl]-aziridine; 1,3-bis(1-aziridinyl)-2-propanol; 1,3-bis(2-methyl-1-aziridinyl)-2-propanol; (1-aziridinylpyruvoyl)-,1-[(p-nitrophenyl)hydrazone] aziridine; and 1,1'-(1,3-dioxo-1,3-propanediyl) bis-aziridine, comprising providing a hyaluronan solution at a pH of 4 to 10, and reacting the hyaluronan with the polyfunctional cross-linking agent.

8. A process of making a compound comprising hyaluronan cross-linked with a polyfunctional cross-linking agent having two or more aziridines selected

from the group consisting of 1,1',1''-methylidynetris-aziridine; 1,1',1''-methylidynetris[2,2-dimethyl]-aziridine; 1,1'-[2-(1-aziridinylmethyl)-1,3-propanediyl]bis-aziridine; 1-aziridinepropanoic acid, 2,2-bis[[3-(1-aziridinyl)-1-oxopropoxy]methyl]-1,3-propanediyl ester; 1-Aziridinepropanoic acid, 2-propyl-, 2-(hydroxymethyl)-2-[[1-oxo-3-(2-propyl-1-aziridinyl)propoxy]methyl]-1,3-propanediyl ester; 1-aziridinepropanoic acid, 2,2-dimethyl-, 2-[[3-(2,2-dimethyl-1-aziridinyl)-1-oxopropoxy]ethyl]-2-(hydroxymethyl)-1,3-propanediyl ester; di[2-(1-aziridinyl)ethyl)]adipate; 1,3-bis(1-aziridinyl)-3-phenyl-1-propanol; 1,1'-(1,3-propanediyl)bis-2-aziridinecarbonitrile; α, β-bis(1-aziridinyl) 2-furanpropanol; 1-[3-(1-aziridinyl)propionyl]-aziridine; 1,3-bis(1-aziridinyl)-2-propanol; 1,3-bis(2-methyl-1-aziridinyl)-2-propanol; (1-aziridinylpyruvoyl)-,1-[(p-nitrophenyl)hydrazone] aziridine; and 1,1'-(1,3-dioxo-1,3-propanediyl) bis-aziridine, comprising reacting hyaluronan with the polyfunctional cross-linking agent at a equivalent ratio of hyaluronan to aziridine of 1:1 to 1:10.

9. The process of claim 8 further comprising a step of adding a pharmacolgically active agent to the hyaluronan before reacting with the polyfunctional cross-linking agent.

10. The process of claim 8 further comprising a step of adding a pharmacolgically active agent to the compound comprising hyaluronan cross-linked with a polyfunctional cross-linking agent.

11. The process of claim 8 wherein the polyfunctional cross-linking agent has two aziridines.

12. The process of claim 8 wherein the polyfunctional cross-linking agent has three aziridines.

13. The process of claim 11 wherein the polyfunctional cross-linking agent is di[2-(1-aziridinyl)ethyl)]adipate.

14. The process of claim 8 further comprising the step of selecting hyaluronan having a molecular weight of 500 kDaltons or more to cross-link with the polyfunctional cross-linking agent.

15. The compound produced by the process of claim 8.

16. The pharmaceutical composition comprising the compound of claim 1 and a pharmacologically active agent.

17. A method of preventing post-operative surgical adhesions of tissue comprising providing the tissue surfaces involved in said surgery with a hydrolyzable coating comprising a compound comprising hyaluronan cross-linked with a polyfunctional cross-linking agent having two or more aziridines, wherein the equivalent ratio of hyaluronan to aziridine is 1:1 to 1:10.

18. The method of claim 17 where the coating is in the form selected from the group consisting of a gel, membrane, foam, and fiber.

19. The method of claim 18 where the coating comprises a pharmacologically active agent.

20. A method of viscosupplementation for medical purposes which comprises contacting body tissue with a biocompatible viscoelastic gel slurry comprising a compound comprising hyaluronan cross-linked with a polyfunctional cross-linking agent having two or more

aziridines, wherein the equivalent ratio of hyaluronan to aziridine is 1:1 to 1:10.

21. The method of claim 20 where the gel slurry further comprises a pharmacologically active agent.